Medical Necessity Guidelines:
Genetic and Molecular Diagnostic Testing

Effective: January 1, 2021

Prior Authorization Required If REQUIRED, submit supporting clinical documentation pertinent to service request.	**Yes ☒ No ☐**

Applies to:

COMMERCIAL Products

☒ Tufts Health Plan Commercial products; Fax: 617.972.9409

☒ Tufts Health Freedom Plan products; Fax: 617.972.9409

- CareLink℠ – Refer to CareLink Procedures, Services and Items Requiring Prior Authorization

TUFTS HEALTH PUBLIC PLANS Products

☒ Tufts Health Direct – A Massachusetts Qualified Health Plan (QHP) (a commercial product); Fax:888.415.9055

☒ Tufts Health Together – MassHealth MCO Plan and Accountable Care Partnership Plans; Fax: 888.415.9055

☒ Tufts Health RITogether – A Rhode Island Medicaid Plan; Fax: 857.304.6404

☒ Tufts Health Unify* – OneCare Plan (a dual-eligible product); Fax: 857.304.6304

*The MNG applies to Tufts Health Unify members unless a less restrictive LCD or NCD exists.

SENIOR Products

- Tufts Health Plan Senior Care Options (SCO), (a dual-eligible product) – Refer to the Tufts Health Plan SCO Prior Authorization List
- Tufts Medicare Preferred HMO, (a Medicare Advantage product) – Refer to the Tufts Medicare Preferred HMO Prior Authorization and Inpatient Notification List

To obtain InterQual® SmartSheets™:

- **Tufts Health Plan Commercial Plan products and Tufts Health Freedom Plan products:** If you are a registered Tufts Health Plan provider click here to access the Provider website. If you are not a Tufts Health Plan provider please click on the Provider Log-in and follow instructions to register on the Provider website or call Provider Services at 888.884.2404.
- **Tufts Health Public Plans products:** InterQual SmartSheet(s) available as part of the prior authorization process.

Note: While you may not be the provider responsible for obtaining prior authorization, as a condition of payment you will need to make sure that prior authorization has been obtained.

OVERVIEW

Tufts Health Plan covers medically necessary genetic and molecular diagnostic testing. Certain prenatal and newborn testing is covered without prior authorization. (See listing of CPT/HCPCS codes covered without prior authorization below).

Prior authorization is required for all other genetic and molecular diagnostic testing. See the listing for tests/codes that require prior authorization below. Refer to Medical Necessity Guidelines: Noncovered Investigational Services for genetic tests which are considered investigational and therefore not covered.

Genetic testing is used to confirm or rule out a suspected genetic condition that may prove pathological and/or to determine a person's chance of developing or passing on a genetic disorder. Cytogenetics examines chromosomes of a single gene to identify structural abnormalities, e.g. deletions, insertions, translocations and amplifications, and is used to detect inherited genetic markers for certain diseases and disorders.

Molecular diagnostic testing is direct DNA analysis used to detect abnormalities in gene sequence and used to determine prognosis and/or to predict response to treatment. Next-generation sequencing

(NGS) allows sequencing of large amounts of DNA and includes select gene sequencing, whole exome sequencing and whole genome sequencing.

Tufts Health Plan uses ChangeHealthcare InterQual Molecular Diagnostics criteria when reviewing prior authorization requests for coverage of most genetic and molecular diagnostic test(s). A completed InterQual SmartSheet must be submitted along with the completed Genetic and Molecular Diagnostics Testing Authorization Request Form and faxed to the appropriate fax number listed above according to Plan. Include all relevant clinical information as applicable.

Tufts Health Plan will continue to use internally developed criteria for the following genetic tests:

- Genetic Testing: BRCA-Related Breast and/or Ovarian Cancer Syndrome
- Genetic Testing: Gene Expression for Cancer of Unknown Primary
- For myRisk® Hereditary Cancer test requests, refer to Genetic Testing: BRCA-Related Breast and/or Ovarian Cancer Syndrome MNG or submit completed Interqual SmartSheet for Lynch Syndrome per above instructions. If criteria for either is met, requests for myRisk® Hereditary Cancer test will be authorized. Refer to CODES section of MNG for applicable CPT code(s).

The following Coverage Guidelines apply to **ALL** prior authorization requests for genetic and molecular diagnostic testing:

CLINICAL COVERAGE CRITERIA

Tufts Health Plan may authorize coverage for specific genetic testing, for a Member, when the Member meets **ALL** of the following criteria:

- The Member falls within a high-risk group for a particular disease(s) based on personal history, family history, documentation of a genetic mutation, and/or ethnic background.
- Patient history, physical examination and conventional diagnostic testing do not result in a definitive diagnosis of suspected disorder.
- The testing method is considered a scientifically proven method for the identification of a specific genetically linked inheritable disease (i.e., the genotypes to be detected by a genetic test must be shown by scientifically valid methods to be associated with the occurrence of a specific disease, and the observations must be independently replicated and subject to peer review).
- InterQual coverage criteria for requested genetic/molecular diagnostic test is met.
- Supporting documentation, including a letter of medical necessity supporting the request for genetic testing, including a review of current clinical scenario, risk factors, and Member's family history, is provided.
    - Documentation must indicate how the results of the genetic test will directly alter the treatment and/or medical management of the Member's diagnosed condition and/or the Member's current pregnancy.
    - For **genetic testing**, counseling by an MD geneticist or a board-certified genetic counselor.
    - Requests and documentation for **molecular diagnostics** can be submitted by an MD with expertise in treatment of the targeted disease.
    - **Medical necessity letters or genetic testing request forms submitted by the performing lab and signed by the requesting provider will not be accepted as sole documentation.**

TUFTS HEALTH PLAN MODIFICATION TO INTERQUAL

Thyroid nodule testing- For the following SmartSheets:

- Afirma Gene Expression Classifier
- Multi-Gene Panel for Thyroid Nodule

Section 10: Bethesda III, atypia or follicular lesion of undetermined significance (AUS/FLUS)

Criteria 1.A- Repeat FNA is not required (consider criteria point met)

Section 20: Bethesda IV, suspicious for follicular or Hürthle cell neoplasm (SFN/SHCN) or follicular neoplasm (FN)

Criteria 1.A – Repeat FNA is not required (consider criteria point met)

BACKGROUND

Genetic testing can provide information about a person's genes and chromosomes. There are many types of genetic testing.

Diagnostic testing identifies or rules out a specific genetic or chromosomal condition. In many cases, genetic testing confirms a diagnosis when a particular condition is suspected based on physical signs and symptoms. Diagnostic testing can be performed before birth or at any time during a person's life, but may not be available for certain genes or genetic conditions. The results of a diagnostic test can influence a person's choices about health care and the management of the disorder.

Carrier testing is used to identify people who carry a gene mutation that can increase the risk of having a child with a genetic disorder. This type of testing is offered to individuals who have a family history of a genetic disorder and to people in certain ethnic groups with an increased risk of specific genetic disorders.

Prenatal testing detects changes in a fetus's genes or chromosomes before birth. This type of testing is offered during pregnancy when there is an increased risk that the baby will have a genetic or chromosomal disorder.

Newborn screening just after birth identifies genetic disorders that can be treated early in life. Most state governments mandate coverage of several of these tests. Tufts Health Plan covers many of these tests without prior authorization.

Preimplantation testing, also called preimplantation genetic diagnosis (PGD), is a specialized technique to detect genetic changes in embryos created using assisted reproductive techniques, such as in-vitro fertilization. Refer to Medical Necessity Guidelines: Preimplantation Genetic Diagnosis (PGD).

Predictive and presymptomatic types of testing detect gene mutations associated with disorders that appear after birth, often later in life. These tests can be helpful to people who have a family member with a genetic disorder, but who have no features of the disorder themselves at the time of testing. Predictive testing can identify mutations that increase a person's risk of developing disorders with a genetic basis, such as certain types of cancer. Presymptomatic testing can determine whether a person will develop a genetic disorder, before any signs or symptoms appear. The results of predictive and presymptomatic testing can provide information about a person's risk of developing a specific disorder and may help with making decisions about medical care.

Targeted gene panels provide sequence data for a limited subset of genes. Analysis of tumor tissue or non-tumor tissue to identify genetic abnormalities may yield actionable findings which can guide treatment decisions, including molecularly targeted therapies.

Additional definitions:

- High Risk Group: individual with personal or family history of an autosomal dominant, autosomal recessive, X-linked recessive or X-linked dominant condition or an individual with a family history of a chromosomal abnormality including a chromosomal translocation or inversion.
- First Degree Relative: An individual's parents, siblings, and children.
- Second Degree Relatives: An individual's grandparents, aunts, uncles, half-siblings, nieces, nephews, and grandchildren.
- Third Degree Relatives: An individual's first cousins, great-grandparents, great-grandchildren, great aunts and great uncles,
- Also for the purposes of genetic testing, relatives are on the same side of the family.

LIMITATIONS

- Testing for the purposes of confirming a suspected diagnosis of a disorder that can be diagnosed based on clinical evaluations alone will not be covered.
- **Genetic tests whose clinical utility is scientifically unproven. Refer to the** Noncovered Investigational Services Medical Necessity Guidelines.
- Testing for conditions which cannot be altered by treatment or prevented by specific interventions will not be covered.
- Testing solely for the purpose of informing the care or management of Member's family member(s) will not be covered. Refer to Genetic Testing: Prenatal, Preconception Medical Necessity Guidelines for prenatal/preconception genetic testing requests.
- Testing must be performed at a contracting laboratory when available.

- A duplicate genetic test for an inherited condition unless there is uncertainty about the validity of the existing test result.[1]
- For testing panels, including but not limited to, multiple genes and/or multiple conditions, in cases where a tiered approach/method is clinically available, testing would be covered ONLY for the number of genes or test(s) that are reasonable and necessary to obtain necessary information for therapeutic decision making and **not** the entire panel.
- Targeted multi-gene panel testing 5-51 genes (CPT 81445 and 81450) for indications other than those listed below (NSCLC and AML).

CODES

The following CPT/HCPCS codes require prior authorization:

- This list of codes may not be all-inclusive.
- Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement

Code	Description
81107	Human platelet Antigen 3 genotyping (HPA-3) ITGA2B integrin, alpha 2b [platelet gyycoprotein IIIb of IIIb/IIIa complex], antigen CD41 [GPIIb]) (eg, neonatal alloimmune thrombocytopenia [NAIT], post-transfusion purpura), gene analysis, common variant, HPA-3a/b (I843S)
81108	Human Platelet Antigen 4 genotyping (HPA-4) ITGB3 (integrin, beta 3 [platelet glycoprotein IIIa], antigen CD61 [GPIIIa]) (eg, neonatal alloimmune thrombocytopenia [NAIT]. Post-transfusion purpura), gene analysis, common variant, HPA-4a/b (R143Q)
81109	Human Platelet Antigen 5 genotyping (HPA-5) ITGA2 (integrin, alpha 2 [CD49B, alpha 2 subunit of VLA-2 receptor] {Gpla)] 9eg, neonatal alloimmune thrombocytopenia [NAIT], post-transfusion purpura), gene analysis, common variant (eg, HPA-5a/b (K505e))
81110	Human Platelet Antigen 6 genotyping (HPA-6w), ITGB3 (integrin , beta 3 [platelet glycoprotein IIIa, antigen CD61] (GPIIIa)) (eg, neonatal alloimmune thrombocytopenia [NAIT], post-transfusion purpura) gene analysis, common variant, HPA-6a/b (r489Q)
81111	Human Platelet Antigen 9 genotyping (HPA-9w), ITGA2B (integrin, alph 2b [platelet glycoprotein IIIb of IIIb/IIIa complex, antigen CD41] [GpIIb]) (eg, neonatal alloimmune thromocytopenia [NAIT], post-transfusion purpura), gene analysis, common variant, HPA-9a/b (V837M)
81112	Human Platelet Antigen 15 genotyping (HPA-15), CD109 (CD109 molecule) (eg, neonatal alloimmune thrombocytopenia [NAIT], post-transfusion purpura), gene analysis, common variant, HPA-15a/b (S682Y)
81120	IDH1 (isocitrate dehydrogenase 1 [NADP+], soluable) (eg, glioma), common variants (eg, R132H, R132C)
81121	IDH2 (isocitrate dehydrogenase 2 [NADP+], soluable) (eg, glioma), common variants (eg, R140W, R172M)
81161	DMD (dystrophin) (e.g., Duchenne/Becker muscular dystrophy) deletion analysis, and duplication analysis, if performed
81168	CCND1/IGH (t(11;14)) (eg, mantle cell lymphoma) translocation analysis, major breakpoint, qualitative and quantitative, if performed
81170	ABL1 (ABL proto-oncogene 1, non-receptor tyrosine kinase) (e.g., acquired imatinib tyrosine kinase inhibitor resistance), gene analysis, variants in the kinase domain
81171	AFF2 (AF4/FMR2 family, member 2 [FMR2]) (eg, fragile X mental retardation 2 [FRAXE]) gene analysis; evaluation to detect abnormal (eg, expanded) alleles

[1] Choosing Wisely®, an initiative of the American Board of Internal Medicine (AIBM) Foundation. Five things physicians and patients should question. The American College of Medical Genetics and Genomics. July 10, 2015.

Code	Description
81172	AFF2 (AF4/FMR2 family, member 2 [FMR2]) (eg, fragile X mental retardation 2 [FRAXE]) gene analysis; characterization of alleles (eg, expanded size and methylation status)
81173	AR (androgen receptor) (eg, spinal and bulbar muscular atrophy, Kennedy disease, X chromosome inactivation) gene analysis; full gene sequence
81174	AR (androgen receptor) (eg, spinal and bulbar muscular atrophy, Kennedy disease, X chromosome inactivation) gene analysis; known familial variant
81175	ASXL 1 (additional sex combs like 1, transcriptional regulator) (eg, myelodysplastic syndrome, myeloproliferative neoplasms, chronic myelomonocytic leukemia), gene analysis; full gene sequence
81176	ASXL 1 (additional sex combs like 1, transcriptional regulator) (eg, myelodysplastic syndrome, myeloproliferative neoplasms, chronic myelomonocytic leukemia), gene analysis; targeted sequence analysis (eg, exon 12)
81177	ATN1 (atrophin 1) (eg, dentatorubral-pallidoluysian atrophy) gene analysis, evaluation to detect abnormal (eg, expanded) alleles
81178	ATXN1 (ataxin 1) (eg, spinocerebellar ataxia) gene analysis, evaluation to detect abnormal (eg, expanded) alleles
81179	ATXN2 (ataxin 2) (eg, spinocerebellar ataxia) gene analysis, evaluation to detect abnormal (eg, expanded) alleles
81180	ATXN3 (ataxin 3) (eg, spinocerebellar ataxia, Machado-Joseph disease) gene analysis, evaluation to detect abnormal (eg, expanded) alleles
81181	ATXN7 (ataxin 7) (eg, spinocerebellar ataxia) gene analysis, evaluation to detect abnormal (eg, expanded) alleles
81182	ATXN8OS (ATXN8 opposite strand [non-protein coding]) (eg, spinocerebellar ataxia) gene analysis, evaluation to detect abnormal (eg, expanded) alleles
81183	ATXN10 (ataxin 10) (eg, spinocerebellar ataxia) gene analysis, evaluation to detect abnormal (eg, expanded) alleles
81184	CACNA1A (calcium voltage-gated channel subunit alpha1 A) (eg, spinocerebellar ataxia) gene analysis; evaluation to detect abnormal (eg, expanded) alleles
81185	CACNA1A (calcium voltage-gated channel subunit alpha1 A) (eg, spinocerebellar ataxia) gene analysis; full gene sequence
81186	CACNA1A (calcium voltage-gated channel subunit alpha1 A) (eg, spinocerebellar ataxia) gene analysis; known familial variant
81187	CNBP (CCHC-type zinc finger nucleic acid binding protein) (eg, myotonic dystrophy type 2) gene analysis, evaluation to detect abnormal (eg, expanded) alleles
81188	CSTB (cystatin B) (eg, Unverricht-Lundborg disease) gene analysis; evaluation to detect abnormal (eg, expanded) alleles
81189	CSTB (cystatin B) (eg, Unverricht-Lundborg disease) gene analysis; full gene sequence
81190	CSTB (cystatin B) (eg, Unverricht-Lundborg disease) gene analysis; known familial variant(s)
81191	NTRK1 (neurotrophic receptor tyrosine kinase 1) (eg, solid tumors) translocation analysis
81192	NTRK2 (neurotrophic receptor tyrosine kinase 2) (eg, solid tumors) translocation analysis
81193	NTRK3 (neurotrophic receptor tyrosine kinase 3) (eg, solid tumors) translocation analysis
81194	NTRK (neurotrophic-tropomyosin receptor tyrosine kinase 1, 2, and 3) (eg, solid tumors) translocation analysis
81201	APC (adenomatous polyposis coli) (e.g., familial adenomatosis polyposis [FAP], attenuated FAP) gene analysis; full gene sequence
81202	APC (adenomatous polyposis coli) (e.g., familial adenomatosis polyposis [FAP], attenuated FAP) gene analysis; known familial variants
81203	APC (adenomatous polyposis coli) (e.g., familial adenomatosis polyposis [FAP], attenuated FAP) gene analysis; duplication/deletion variants

Code	Description
81204	AR (androgen receptor) (eg, spinal and bulbar muscular atrophy, Kennedy disease, X chromosome inactivation) gene analysis; characterization of alleles (eg, expanded size or methylation status)
81206	*BCR/ABL1 (t(9;22))* (e.g., chronic myelogenous leukemia) translocation analysis; major breakpoint, qualitative or quantitative
81207	*BCR/ABL1 (t(9;22))* (e.g., chronic myelogenous leukemia) translocation analysis; minor breakpoint, qualitative or quantitative
81208	*BCR/ABL1 (t(9;22))* (e.g., chronic myelogenous leukemia) translocation analysis; major breakpoint, other breakpoint, qualitative or quantitative
81210	BRAF (V-RAF Murine Sarcoma Viral Oncogene Homolog B1) (e.g., colon cancer, gene analysis, V600E variant)
81218	CEBPA (CCAAT/enhancer binding protein [C/EBP], alpha) (e.g., acute myeloid leukemia), gene analysis, full gene sequence
81219	CALR (calreticulin) (e.g., myeloproliferative disorders), gene analysis, common variants in exon 9
81225	CYP2C19 (cytochrome P450, family 2, subfamily C, polypeptide 19) (e.g., drug metabolism), gene analysis, common variants (e.g., *2, *3, *4, *8, *17)
81226	CYP2D6 (cytochrome P450, family 2, subfamily D, polypeptide 6) (e.g., drug metabolism), gene analysis, common variants (e.g., *2, *3, *4, *5, *6, *9, *10, *17, *19, *29, *35, *41, *1XN, *2XN, *4XN)
81227	CYP2C9 (cytochrome P450, family 2, subfamily C, polypeptide 9) (e.g., drug metabolism), gene analysis, common variants (e.g., *2, *3, *5, *6)
81228	Cytogenomic constitutional (genome-wide) microarray analysis; interrogation of genomic regions for copy number variants (e.g., Bacterial Artificial Chromosome [BAC] or oligo-based comparative genomic hybridization [CGH] microarray analysis)
81229	Cytogenomic constitutional (genome-wide) microarray analysis; interrogation of genomic regions for copy number and single nucleotide polymorphism (SNP) variants for chromosomal abnormalities
81233	BTK (Bruton's tyrosine kinase) (eg, chronic lymphocytic leukemia) gene analysis, common variants (eg, C481S, C481R, C481F)
81234	DMPK (DM1 protein kinase) (eg, myotonic dystrophy type 1) gene analysis; evaluation to detect abnormal (expanded) alleles
81236	EZH2 (enhancer of zeste 2 polycomb repressive complex 2 subunit) (eg, myelodysplastic syndrome, myeloproliferative neoplasms) gene analysis, full gene sequence
81237	EZH2 (enhancer of zeste 2 polycomb repressive complex 2 subunit) (eg, diffuse large B-cell lymphoma) gene analysis, common variant(s) (eg, codon 646)
81238	F9(coagulation factor IX) (eg, hemophilia B) full gene sequence
81239	DMPK (DM1 protein kinase) (eg, myotonic dystrophy type 1) gene analysis; characterization of alleles (eg, expanded size)
81240	F2 (prothrombin, coagulation factor II) (e.g., hereditary hypercoagulability) gene analysis, 20210G>A variant
81241	F5 (coagulation Factor V) (e.g., hereditary hypercoagulability) gene analysis, Leiden variant
81243	FMR1 (Fragile X mental retardation 1) (e.g., fragile X mental retardation) gene analysis; evaluation to detect abnormal (e.g., expanded) alleles
81244	characterization of alleles (e.g., expanded size and promoter methylation status)
81245	FLT3 (fms-related tyrosine kinase 3) (e.g., acute myeloid leukemia), gene analysis, internal tandem duplication (ITD) variants (i.e., exons 14, 15)
81246	FLT3 (fms-related tyrosine kinase 3) (e.g., acute myeloid leukemia), gene analysis; tyrosine kinase domain (TKD) variants (e.g., D835, I836)

Code	Description
81247	G6PD (glucose-6-phosphate dehydrogenase) (eg, hemolytic anemia, jaundice), gene analysis; common variant(s) (eg, A, A-)
81248	G6PD (glucose-6-phosphate dehydrogenase) (eg, hemolytic anemia, jaundice), gene analysis; known familial variant(s)
81249	G6PD (glucose-6-phosphate dehydrogenase) (eg, hemolytic anemia, jaundice), gene analysis; full gene sequence
81256	HFE (hemochromatosis) (e.g., hereditary hemochromatosis) gene analysis, common variants (e.g., C282Y, H63D)
81257	HBA1/HBA2 (alpha globin 1 and alpha globin 2) (e.g., alpha thalassemia, Hb Bart hydrops fetalis syndrome, HbH disease), gene analysis, for common deletions or variant (e.g., Southeast Asian, Thai, Filipino, Mediterranean, alpha3.7, alpha4.2, alpha20.5, and Constant Spring)
81258	HBA1/HBA2 (alpha globin 1 and alpha globin 2) (eg, alpha thalassemia, Hb Bart hydrops fetalis syndrome, Hbh disease), gene analysis; known familial variant
81259	HBA1/HBA2 (alpha globin 1 and alpha globin 2) (eg, alpha thalassemia, Hb Bart hydrops fetalis syndrome, Hbh disease), gene analysis; full gene sequence
81261	IGH@ (Immunoglobulin heavy chain locus) (e.g., leukemias and lymphomas, B-cell), gene rearrangement analysis to detect abnormal clonal population(s); amplified methodology (e.g., polymerase chain reaction)
81262	IGH@ (Immunoglobulin heavy chain locus) (e.g., leukemias and lymphomas, B-cell), gene rearrangement analysis to detect abnormal clonal population(s); direct probe methodology (e.g., Southern blot)
81263	IGH@ (Immunoglobulin heavy chain locus) (e.g., leukemia and lymphoma, B-cell), variable region somatic mutation analysis
81264	IGK@ (Immunoglobulin kappa light chain locus) (e.g., leukemia and lymphoma, B-cell), gene rearrangement analysis, evaluation to detect abnormal clonal population(s)
81269	HBA1/HBA2 (alpha globin 1 and alpha globin 2) (eg, alpha thalassemia, Hb Bart hydrops fetalis syndrome, Hbh disease), gene analysis; duplication/deletion variants
81270	JAK2 (Janus kinase 2) (e.g., myeloproliferative disorder) gene analysis, p.Val617Phe (V617F) variant
81271	HTT (huntingtin) (eg, Huntington disease) gene analysis; evaluation to detect abnormal (eg, expanded) alleles
81272	KIT (v-kit Hardy-Zuckerman 4 feline sarcoma viral oncogene homolog) (e.g., gastrointestinal stromal tumor [GIST], acute myeloid leukemia, melanoma), gene analysis, targeted sequence analysis (e.g., exons 8, 11, 13, 17, 18)
81273	KIT (v-kit Hardy-Zuckerman 4 feline sarcoma viral oncogene homolog) (e.g., mastocytosis), gene analysis, D816 variant(s)
81274	HTT (huntingtin) (eg, Huntington disease) gene analysis; characterization of alleles (eg, expanded size)
81275	KRAS(V-KI-RAS2 Kirsten Rat Sarcoma viral oncogene) gene analysis, variants in codons 12 and 13
81276	KRAS (Kirsten rat sarcoma viral oncogene homolog) (e.g., carcinoma) gene analysis; additional variant(s) (e.g., codon 61, codon 146)
81278	IGH@/BCL2 (t(14;18)) (eg, follicular lymphoma) translocation analysis, major breakpoint region (MBR) and minor cluster region (mcr) breakpoints, qualitative or quantitative
81279	JAK2 (Janus kinase 2) (eg, myeloproliferative disorder) targeted sequence analysis (eg, exons 12 and 13)
81283	IFNL3 (interferon, lambda 3) (eg, drug response), gene analysis, rs12979860 variant

Code	Description
81287	MGMT (O-6-methylguanine-DNA methyltransferase) (eg, glioblastoma multiforme), promoter methylation analysis
81288	MLH1 (mutL homolog 1, colon cancer, nonpolyposis type 2) (e.g., hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; promoter methylation analysis
81292	MLH1 (mutL homolog 1, colon cancer, nonpolyposis type 2) (e.g., hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; full sequence analysis
81293	MLH1 (mutL homolog 1, colon cancer, nonpolyposis type 2) (e.g., hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; known familial variants
81294	MLH1 (mutL homolog 1, colon cancer, nonpolyposis type 2) (e.g., hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; duplication/deletion variants
81295	MSH2 (mutS homolog 2, colon cancer, nonpolyposis type 1) (e.g., hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; full sequence analysis
81296	MSH2 (mutS homolog 2, colon cancer, nonpolyposis type 1) (e.g., hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; known familial variants
81297	MSH2 (mutS homolog 2, colon cancer, nonpolyposis type 1) (e.g., hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; duplication/deletion variants
81298	MSH6 (mutS homolog 6 [E. coli]) (e.g., hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; full sequence analysis
81299	MSH6 (mutS homolog 6 [E. coli]) (e.g., hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; known familial variants
81300	MSH6 (mutS homolog 6 [E. coli]) (e.g., hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; duplication/deletion variants
81301	Microsatellite instability analysis of markers for mismatch repair deficiency, includes comparison of neoplastic and normal tissue
81302	MECP2 (methyl CpG binding protein 2) (e.g., Rett syndrome) gene analysis; full sequence analysis
81303	MECP2 (methyl CpG binding protein 2) (e.g., Rett syndrome) gene analysis; known familial variant
81304	MECP2 (methyl CpG binding protein 2) (e.g., Rett syndrome) gene analysis; duplication/deletion variants
81305	MYD88 (myeloid differentiation primary response 88) (eg, Waldenstrom's macroglobulinemia, lymphoplasmacytic leukemia) gene analysis, p.Leu265Pro (L265P) variant
81307	PALB2 (partner and localizer of BRCA2) (eg, breast and pancreatic cancer) gene analysis; full gene sequence
81308	PALB2 (partner and localizer of BRCA2) (eg, breast and pancreatic cancer) gene analysis; known familial variant
81309	PIK3CA (phosphatidylinositol-4, 5-biphosphate 3-kinase, catalytic subunit alpha) (eg, colorectal and breast cancer) gene analysis, targeted sequence analysis (eg, exons 7, 9, 20)
81310	NPM1 (nucleophosmin) (e.g., acute myeloid leukemia) gene analysis, exon 12 variants
81311	NRAS (neuroblastoma RAS viral [v-ras] oncogene homolog) (e.g., colorectal carcinoma), gene analysis, variants in exon 2 (e.g., codons 12 and 13) and exon 3 (e.g., codon 61)
81314	PDGFRA (platelet-derived growth factor receptor, alpha polypeptide) (e.g., gastrointestinal stromal tumor [GIST]), gene analysis, targeted sequence analysis (e.g., exons 12, 18)
81315	PML/RARalpha, (t(15;17)), (promyelocytic leukemia/retinoic acid receptor alpha) (e.g., promyelocytic leukemia) translocation analysis; common breakpoints (e.g., intron 3 and intron 6), qualitative or quantitative

Code	Description
81316	PML/RARalpha, (t(15;17)), (promyelocytic leukemia/retinoic acid receptor alpha) (e.g., promyelocytic leukemia) translocation analysis; single breakpoint (e.g., intron 3, intron 6 or exon 6), qualitative or quantitative
81317	PMS2 (postmeiotic segregation increased 2 [S. cerevisiae]) (e.g., hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; full sequence analysis
81318	PMS2 (postmeiotic segregation increased 2 [S. cerevisiae]) (e.g., hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; known familial variants
81319	PMS2 (postmeiotic segregation increased 2 [S. cerevisiae]) (e.g., hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; duplication/deletion variants
81320	PLCG2 (phospholipase C gamma 2) (eg, chronic lymphocytic leukemia) gene analysis, common variants (eg, R665W, S707F, L845F)
81321	PTEN (phosphatase and tensin homolog) (e.g., Cowden syndrome, PTEN hamartoma tumor syndrome) gene analysis; full sequence analysis
81322	PTEN (phosphatase and tensin homolog) (e.g., Cowden syndrome, PTEN hamartoma tumor syndrome) gene analysis; known familial variant
81323	PTEN (phosphatase and tensin homolog) (e.g., Cowden syndrome, PTEN hamartoma tumor syndrome) gene analysis; duplication/deletion variant
81324	PMP22 (peripheral myelin protein 22) (e.g., Charcot-Marie-Tooth, hereditary neuropathy with liability to pressure palsies) gene analysis; duplication/deletion analysis
81325	PMP22 (peripheral myelin protein 22) (e.g., Charcot-Marie-Tooth, hereditary neuropathy with liability to pressure palsies) gene analysis; full sequence analysis
81326	PMP22 (peripheral myelin protein 22) (e.g., Charcot-Marie-Tooth, hereditary neuropathy with liability to pressure palsies) gene analysis; known familial variant
81331	SNRPN/UBE3A (small nuclear ribonucleoprotein polypeptide N and ubiquitin protein ligase E3A) (e.g., Prader-Willi syndrome and/or Angelman syndrome), methylation analysis
81332	SERPINA1 (serpin peptidase inhibitor, clade A, alpha-1 antiproteinase, antitrypsin, Member 1) (e.g., alpha-1-antitrypsin deficiency), gene analysis, common variants (e.g., *S and *Z)
81333	TGFBI (transforming growth factor beta-induced) (eg, corneal dystrophy) gene analysis, common variants (eg, R124H, R124C, R124L, R555W, R555Q)
81334	RUNX1 (runt related transcription factor 1) (eg, acute myeloid leukemia, familial platelet disorder with associated myeloid malignancy), gene analysis, targeted sequence analysis (eg, exons 3-8)
81338	MPL (MPL proto-oncogene, thrombopoietin receptor) (eg, myeloproliferative disorder) gene analysis; common variants (eg, W515A, W515K, W515L, W515R)
81339	MPL (MPL proto-oncogene, thrombopoietin receptor) (eg, myeloproliferative disorder) gene analysis; sequence analysis, exon 10
81340	TRB@ (T cell antigen receptor, beta) (e.g., leukemia and lymphoma), gene rearrangement analysis to detect abnormal clonal population(s); using amplification methodology (e.g., polymerase chain reaction)
81341	TRB@ (T cell antigen receptor, beta) (e.g., leukemia and lymphoma), gene rearrangement analysis to detect abnormal clonal population(s); using direct probe methodology (e.g., Southern blot)
81342	TRG@ (T cell antigen receptor, gamma) (e.g., leukemia and lymphoma), gene rearrangement analysis, evaluation to detect abnormal clonal population(s)
81343	PPP2R2B (protein phosphatase 2 regulatory subunit Bbeta) (eg, spinocerebellar ataxia) gene analysis, evaluation to detect abnormal (eg, expanded) alleles
81344	TBP (TATA box binding protein) (eg, spinocerebellar ataxia) gene analysis, evaluation to detect abnormal (eg, expanded) alleles

Code	Description
81345	TERT (telomerase reverse transcriptase) (eg, thyroid carcinoma, glioblastoma multiforme) gene analysis, targeted sequence analysis (eg, promoter region)
81347	SF3B1 (splicing factor [3b] subunit B1) (eg, myelodysplastic syndrome/acute myeloid leukemia) gene analysis, common variants (eg, A672T, E622D, L833F, R625C, R625L)
81348	SRSF2 (serine and arginine-rich splicing factor 2) (eg, myelodysplastic syndrome, acute myeloid leukemia) gene analysis, common variants (eg, P95H, P95L)
81350	UGT1A1 (UDP glucuronosyltransferase 1 family, polypeptide A1) (e.g., irinotecan metabolism), gene analysis, common variants (e.g., *28, *36, *37)
81351	TP53 (tumor protein 53) (eg, Li-Fraumeni syndrome) gene analysis; full gene sequence
81352	TP53 (tumor protein 53) (eg, Li-Fraumeni syndrome) gene analysis; targeted sequence analysis (eg, 4 oncology)
81353	TP53 (tumor protein 53) (eg, Li-Fraumeni syndrome) gene analysis; known familial variant
81357	U2AF1 (U2 small nuclear RNA auxiliary factor 1) (eg, myelodysplastic syndrome, acute myeloid leukemia) gene analysis, common variants (eg, S34F, S34Y, Q157R, Q157P)
81360	ZRSR2 (zinc finger CCCH-type, RNA binding motif and serine/arginine-rich 2) (eg, myelodysplastic syndrome, acute myeloid leukemia) gene analysis, common variant(s) (eg, E65fs, E122fs, R448fs)
81361	HBB (hemoglobin, subunit beta) (eg, sickle cell anemia beta thalassemia, hemoglobinopathy); common variant(s) (eg, HbS, HbC, HbE)
81362	HBB (hemoglobin, subunit beta) (eg, sickle cell anemia beta thalassemia, hemoglobinopathy); known familial variant(s)
81363	HBB (hemoglobin, subunit beta) (eg, sickle cell anemia beta thalassemia, hemoglobinopathy); duplication/deletion variant(s)
81364	HBB (hemoglobin, subunit beta) (eg, sickle cell anemia beta thalassemia, hemoglobinopathy); full gene sequence
81370	HLA Class I and II typing, low resolution (e.g., antigen equivalents): HLA-A, -B, -C, -DRB 1/3/4/5, and –DQB1
81371	HLA Class I and II typing, low resolution (e.g., antigen equivalents): *HLA-A, -B, and –DRB1* (e.g. verification typing)
81372	HLA Class I typing, low resolution (e.g., antigen equivalents); complete (i.e., HLA-A, -B, and-C)
81373	HLA Class I typing, low resolution (e.g., antigen equivalents); one locus (*e.g. HLA-A, -B, or –C*), each
81374	HLA Class I typing, low resolution (e.g., antigen equivalents); one antigen equivalent (e.g. B*27), each
81375	HLA Class II typing, low resolution (e.g., antigen equivalents); HLA-DRB1/3/4/5 and –DQB1
81376	HLA Class II typing, low resolution (e.g., antigen equivalents); one locus (*e.g. HLA-DRB1, -DRB3/4/5, -DQB1, -DQA1, -DPB1, or –DPA1*), each
81377	HLA Class II typing, low resolution (e.g., antigen equivalents); one antigen equivalent , each
81378	HLA Class I and II typing, high resolution (i.e., alleles or allele groups), HLA-A, -B, -C, and -DRB1
81379	HLA Class I typing, high resolution (i.e., alleles or allele groups); complete (i.e., HLA-A, -B, and -C)
81380	HLA Class I typing, high resolution (i.e., alleles or allele groups); 1 locus (e.g., HLA-A, -B, or -C), each

Code	Description
81381	HLA Class I typing, high resolution (i.e., alleles or allele groups); 1 allele or allele group (e.g., B*57:01P), each
81382	HLA Class II typing, high resolution (i.e., alleles or allele groups); one locus (e.g., *HLA-DRB1, - DRB3, 4/5, -DQB1, -DQA1, -DPB1,* or *-DPA1*), each
81383	HLA Class II typing, high resolution (i.e., alleles or allele groups); 1 allele or allele group (e.g., HLA-DQB1*06:02P), each
81400	Molecular pathology procedure, Level 1 (e.g., identification of single germline variant [e.g., SNP] by techniques such as restriction enzyme digestion or melt curve analysis)
81401	Molecular pathology procedure, Level 2 (e.g., 2-10 SNPs, 1 methylated variant, or 1 somatic variant [typically using nonsequencing target variant analysis], or detection of a dynamic mutation disorder/triplet repeat)
81402	Molecular pathology procedure, Level 3 (e.g., > 10 SNPs, 2-10 methylated variants, or 2-10 somatic variants [typically using non-sequencing target variant analysis], immunoglobulin and T-cell receptor gene rearrangements, duplication/deletion variants 1 exon)
81403	Molecular pathology procedure, Level 4 (e.g., analysis of single exon by DNA sequence analysis, analysis of > 10 amplicons using multiplex PCR in 2 or more independent reactions, mutation scanning or duplication/deletion variants of 2-5 exons)
81404	Molecular pathology procedure, Level 5 (e.g., analysis of 2-5 exons by DNA sequence analysis, mutation scanning or duplication/deletion variants of 6-10 exons, or characterization of a dynamic mutation disorder/triplet repeat by Southern blot analysis)
81405	Molecular pathology procedure, Level 6 (e.g., analysis of 6-10 exons by DNA sequence analysis, mutation scanning or duplication/deletion variants of 11-25 exons)
81406	Molecular pathology procedure, Level 7 (e.g., analysis of 11-25 exons by DNA sequence analysis, mutation scanning or duplication/deletion variants of 26-50 exons, cytogenomic array analysis for neoplasia)
81407	Molecular pathology procedure, Level 8 (e.g., analysis of 26-50 exons by DNA sequence analysis, mutation scanning or duplication/deletion variants of > 50 exons, sequence analysis of multiple genes on 1 platform)
81408	Molecular pathology procedure, Level 9 (e.g., analysis of > 50 exons in a single gene by DNA sequence analysis)
81410	Aortic dysfunction or dilation (e.g., Marfan syndrome, Loeys Dietz syndrome, Ehler Danlos syndrome type IV, arterial tortuosity syndrome); genomic sequence analysis panel, must include sequencing of at least 9 genes, including FBN1, TGFBR1, TGFBR2, COL3A1, MYH11, ACTA2, SLC2A10, SMAD3, and MYLK
81411	Aortic dysfunction or dilation (e.g., Marfan syndrome, Loeys Dietz syndrome, Ehler Danlos syndrome type IV, arterial tortuosity syndrome); duplication/deletion analysis panel, must include analyses for TGFBR1, TGFBR2, MYH11, and COL3A1
81413	Cardiac ion channelopathies (eg, Brugada syndrome, long QT syndrome, short QT syndrome, catecholaminergic polymorphic ventricular tachycardia); genomic sequence analysis panel, must include sequencing of at least 10 genes, including ANK2, CASQ2, CAV3, KCNE1, KCNE2, KCNH2, KCNJ2, KCNQ1, RYR2, and SCN5A
81414	Cardiac ion channelopathies (eg, Brugada syndrome, long QT syndrome, short QT syndrome, catecholaminergic polymorphic ventricular tachycardia); duplication/deletion gene analysis panel, must include analysis of at least 2 genes, including KCNH2 and KCNQ1
81434	Hereditary retinal disorders (eg, retinitis pigmentosa, Leber congenital amaurosis, cone-rod dystrophy), genomic sequence analysis panel, must include sequencing of at least 15 genes, including ABCA4, CNGA1, CRB1, EYS, PDE6A, PDE6B, PRPF31, PRPH2, RDH12, RHO, RP1, RP2, RPE65, RPGR, and USH2A

Code	Description
81435	Hereditary colon cancer syndromes (e.g., Lynch syndrome, familial adenomatosis polyposis); genomic sequence analysis panel, must include analysis of at least 7 genes, including APC, CHEK2, MLH1, MSH2, MSH6, MUTYH, and PMS2
81436	Hereditary colon cancer syndromes (e.g., Lynch syndrome, familial adenomatosis polyposis); duplication/deletion gene analysis panel, must include analysis of at least 8 genes, including APC, MLH1, MSH2, MSH6, PMS2, EPCAM, CHEK2, and MUTYH
81437	Hereditary neuroendocrine tumor disorders (e.g., medullary thyroid carcinoma, parathyroid carcinoma, malignant pheochromocytoma or paraganglioma); genomic sequence analysis panel, must include sequencing of at least 6 genes, including MAX, SDHB, SDHC, SDHD, TMEM127, and VHL
81438	Hereditary neuroendocrine tumor disorders (e.g., medullary thyroid carcinoma, parathyroid carcinoma, malignant pheochromocytoma or paraganglioma); duplication/deletion analysis panel, must include analyses for SDHB, SDHC, SDHD, and VHL
81439	Inherited cardiomyopathy (eg, hypertrophic cardiomyopathy, dilated cardiomyopathy, arrhythmogenic right ventricular cardiomyopathy) genomic sequence analysis panel, must include sequencing of at least 5 genes, including DSG2, MYBPC3, MYH7, PKP2, and TTN
81443	Genetic testing for severe inherited conditions (eg, cystic fibrosis, Ashkenazi Jewish-associated disorders [eg, Bloom syndrome, Canavan disease, Fanconi anemia type C, mucolipidosis type VI, Gaucher disease, Tay-Sachs disease], beta hemoglobinopathies, phenylketonuria, galactosemia), genomic sequence analysis panel, must include sequencing of at least 15 genes (eg, ACADM, ARSA, ASPA, ATP7B, BCKDHA, BCKDHB, BLM, CFTR, DHCR7, FANCC, G6PC, GAA, GALT, GBA, GBE1, HBB, HEXA, IKBKAP, MCOLN1, PAH
81479	Unlisted molecular pathology procedure
81519	Oncology (breast), mRNA, gene expression profiling by real-time RT-PCR of 21 genes, utilizing formalin-fixed paraffin embedded tissue, algorithm reported as recurrence score (Oncotype DX®, Genomic Health)
81521	Oncology (breast), mRNA, microarray gene expression profiling of 70 content genes and 465 housekeeping genes, utilizing fresh frozen or formalin-fixed paraffin-embedded tissue, algorithm reported as index related to risk of distant metastasis (MammaPrint®, Agendia, Inc)
81541	Oncology (prostate), mRNA gene expression profiling by real-time RT-PCR of 46 genes (31 content and 15 housekeeping), utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as a disease-specific mortality risk score (Prolaris ®, Myriad Genetic Laboratories, Inc.)
81599	Unlisted molecular pathology procedure
84999	Unlisted chemistry procedure
86386	Nuclear Matrix Protein 22 (NMP22), qualitative
S3840	DNA analysis for germline mutations of the RET proto-oncogene for susceptibility to multiple endocrine neoplasia type 2
S3841	Genetic testing for retinoblastoma
S3842	Genetic testing for Von Hippel-Lindau disease
S3845	Genetic testing for alpha-thalassemia
S3846	Genetic testing for hemoglobin E beta-thalassemia
S3850	Genetic testing for sickle cell anemia
S3854	Gene expression profiling panel for use in the management of breast cancer treatment
S3861	Genetic testing, sodium channel, voltage-gated, type V, alpha subunit (SCN5A) and variants for suspected Brugada Syndrome
S3865	Comprehensive gene sequence analysis for hypertrophic cardiomyopathy

Code	Description
S3866	Genetic analysis for a specific gene mutation for hypertrophic cardiomyopathy (HCM) in an individual with a known HCM mutation in the family (Effective 4/1/09)
S3870	Comparative genomic hybrization (CGH) microarray testing for developmental delay, autism spectrum disorder and/or mental retardation (e.g., SignatureChip®)
0016U	Oncology (hematolymphoid neoplasia), RNA, BCR/ABL1 major and minor breakpoint fusion transcripts, quantitative PCR amplification, blood or bone marrow, report of fusion not detected or detected with quantitation (BCR-ABL1 major and minor breakpoint fusion transcripts, University of Iowa, Department of Pathology, Asuragen)
0017U	Oncology (hematolymphoid neoplasia), JAK2 mutation, DNA, PCR amplification of exons 12-14 and sequence analysis, blood or bone marrow, report of JAK2 mutation not detected or detected (JAK2 Mutation, University of Iowa, Department of Pathology)
0022U	Targeted genomic sequence analysis panel, non-small cell lung neoplasia, DNA and RNA analysis, 23 genes, interrogation for sequence variants and rearrangements, reported as presence/absence of variants and associated therapy(ies) to consider (Oncomine™ Dx Target Test, Thermo Fisher Scientific)
0023U	Oncology (acute myelogenous leukemia), DNA, genotyping of internal tandem duplication, p.D835, p.I836, using mononuclear cells, reported as detection or non-detection of FLT3 mutation and indication for or against the use of midostaurin (LeukoStrat® CDx FLT3 Mutation Assay, Invivoscribe Technologies, Inc.)
0026U	Oncology (thyroid), DNA and mRNA of 112 genes, next-generation sequencing, fine needle aspirate of thyroid nodule, algorithmic analysis reported as a categorical result ("Positive, high probability of malignancy" or "Negative, low probability of malignancy") (Thyroseq Genomic Classifier, CBLPath, Inc, University of Pittsburgh Medical Center)
0027U	JAK2 (Janus kinase 2) (eg, myeloproliferative disorder) gene analysis, targeted sequence analysis exons 12-15 (*JAK2* Exons 12 to 15 Sequencing, Mayo Clinic)
0046U	FLT3 (fms-related tyrosine kinase 3) (eg, acute myeloid leukemia) internal tandem duplication (ITD) variants, quantitative (FLT3 ITD MRD by NGS, LabPMM LLC, an Invivoscribe Technologies, Inc. Co.)
0049U	NPM1 (nucleophosmin) (eg, acute myeloid leukemia) gene analysis, quantitative (*NPM1* MRD by NGS, LabPMM LLC, an Invivoscribe Technologies, Inc Company)
0069U	Oncology (colorectal), microRNA, RT-PCR expression profiling of miR-31-3p, formalin-fixed paraffin-embedded tissue, algorithm reported as an expression score (miR-31now™, GoPath Laboratories)
0154U	FGFR3 (fibroblast growth factor receptor 3) gene analysis (ie, p.R248C [c.742C>T], p.S249C [c.746C>G], p.G370C [c.1108G>T], p.Y373C [c.1118A>G], FGFR3-TACC3v1, and FGFR3-TACC3v3) (therascreen® *FGFR* RGQ RT-PCR Kit, QIAGEN, QIAGEN GmbH)
0155U	PIK3CA (phosphatidylinositol-4,5-bisphosphate 3-kinase, catalytic subunit alpha) (eg, breast cancer) gene analysis (ie, p.C420R, p.E542K, p.E545A, p.E545D [g.1635G>T only], p.E545G, p.E545K, p.Q546E, p.Q546R, p.H1047L, p.H1047R, p.H1047Y) (therascreen® *PIK3CA* RGQ PCR Kit, QIAGEN, QIAGEN GmbH)
0172U	Oncology (solid tumor as indicated by the label), somatic mutation analysis of BRCA1 (BRCA1, DNA repair associated), BRCA2 (BRCA2, DNA repair associated) and analysis of homologous recombination deficiency pathways, DNA, formalin-fixed paraffin-embedded tissue, algorithm quantifying tumor genomic instability score (myChoice® CDx, Myriad Genetics Laboratories, Inc, Myriad Genetics Laboratories, Inc)
0177U	Oncology (breast cancer), DNA, PIK3CA (phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha) gene analysis of 11 gene variants utilizing plasma, reported as PIK3CA gene mutation status (therascreen® *PIK3CA* RGQ PCR Kit, QIAGEN, QIAGEN GmbH)

Tufts Health Plan may authorize coverage of targeted multi-gene panel testing for non-small cell lung cancer (NSCLC) and acute myeloid leukemia (AML) when criteria are met. The following InterQual SmartSheets are to be used when requesting prior authorization. The applicable InterQual SmartSheet must be completed and faxed to the appropriate fax number listed above according to Plan.

Targeted multi-gene panel for non-small cell lung cancer (ALK, BRAF, EGFR, PD-L1, ROS1)
The following CPT(s) code requires prior authorization:

CPT Code	Description
81445	Targeted genomic sequence analysis panel, solid organ neoplasm, DNA analysis, and RNA analysis when performed, 5-50 genes (eg, ALK, BRAF, CDKN2A, EGFR, ERBB2, KIT, KRAS, NRAS, MET, PDGFRA, PDGFRB, PGR, PIK3CA, PTEN, RET), interrogation for sequence variants and copy number variants or rearrangements, if performed

AML targeted multi-gene panel (FLT3-ITD, NPM1, CEBPA, RUNX1, TP53, ASXL1, KIT)
The following CPT code(s) requires authorization:

CPT Code	Description
81450	Targeted genomic sequence analysis panel, hematolymphoid neoplasm or disorder, DNA analysis, and RNA analysis when performed, 5-50 genes (eg, BRAF, CEBPA, DNMT3A, EZH2, FLT3, IDH1, IDH2, JAK2, KRAS, KIT, MLL, NRAS, NPM1, NOTCH1), interrogation for sequence variants, and copy number variants or rearrangements, or isoform expression or mRNA expression levels, if performed

The following CPT/HCPCS codes are to be submitted when requesting prior authorization for myRISK™ Hereditary Cancer Test or myRisk Update Test:

Code	Description
81406	Molecular pathology procedure, Level 7 (eg, analysis of 11-25 exons by DNA sequence analysis, mutation scanning or duplication/deletion variants of 26-50 exons, cytogenomic array analysis for neoplasia) (when used for myRISK™ Update Test)
81479	Unlisted molecular pathology procedure (when used for myRISK™ Hereditary Cancer Test)

The following CPT/HCPCS codes DO NOT require prior authorization for female testing

- This list of codes may not be all inclusive.
- Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement

Tufts Health Plan will cover the following genetic tests without prior authorization for female testing:
Refer to **Genetic Testing:** Maternal Tests for Fetal Trisomy MNG**** and/or **Genetic Testing:** Prenatal, Preconception MNG

- Ashkenazi panel (which includes: Tay-Sachs Disease, Gaucher Disease, Cystic Fibrosis, Canavan Disease, Bloom Syndrome, Familial Dysautonomia, Mucolipidosis Type IV, Fanconi Anemia Type C, Nieman-Pick Disease Type A, Maple Syrup Urine Disease, and Glycogen Storage Disease type 1a)
- Cystic Fibrosis, Spinal Muscular Atrophy, Fetal aneuploidy (trisomy 21, 18 and 13)
- First trimester screening combination of ultrasound for nuchal cord translucency and maternal blood testing for free beta subunit of human chorionic gonadotropin (ß-hCG), and pregnancy-associated plasma protein-A (PAPP-A). This testing is also known as Early Risk Assessment, First Screen, or Ultrascreen.
- Second trimester screening combination second-trimester screening using four serum markers (alpha-fetoprotein, ß-hCG, unconjugated estriol, inhibin-A)

Code	Description
81200	ASPA (aspartoacylase) (e.g., Canavan disease) gene analysis, common variants (e.g., E285A, Y231X)

Code	Description
81205	BCKDHB (branched-chain keto acid dehydrogenase E1, beta polypeptide) (e.g., maple syrup urine disease) gene analysis, common variants (e.g., R183P, G278S, E422X)
81209	BLM (Bloom syndrome, RecQ helicase-like) (e.g., Bloom syndrome) gene analysis, 2281del6ins7 variant
81220	CFTR (cystic fibrosis transmembrane conductance regulator) (e.g., cystic fibrosis) gene analysis; common variants (e.g., ACMG/ACOG guidelines)
81221	CFTR (cystic fibrosis transmembrane conductance regulator) (e.g., cystic fibrosis) gene analysis; known familial variants
81222	CFTR (cystic fibrosis transmembrane conductance regulator) (e.g., cystic fibrosis) gene analysis; duplication/deletion variants
81223	CFTR (cystic fibrosis transmembrane conductance regulator) (e.g., cystic fibrosis) gene analysis; full gene sequence
81224	CFTR (cystic fibrosis transmembrane conductance regulator) (e.g., cystic fibrosis) gene analysis; intron 8 poly-T analysis (e.g., male infertility)
81242	FANCC (Fanconi anemia, complementation group C) (e.g., Fanconi anemia, type C) gene analysis, common variant (e.g., IVS4+4A>T)
81250	G6PC (glucose-6-phosphatase, catalytic subunit) (e.g., Glycogen storage disease, type 1a, von Gierke disease) gene analysis, common variants (e.g., R83C, Q347X)
81251	GBA (glucosidase, beta, acid) (e.g., Gaucher disease) gene analysis, common variants (e.g., N370S, 84GG, L444P, IVS2+1G>A)
81255	HEXA (hexosaminidase A [alpha polypeptide]) (e.g., Tay-Sachs disease) gene analysis, common variants (e.g., 1278insTATC, 1421+1G>C, G269S)
81260	IKBKAP (inhibitor of kappa light polypeptide gene enhancer in B-cells, kinase complex-associated protein) (e.g., familial dysautonomia) gene analysis, common variants (e.g., 2507+6T>C, R696P)
81290	MCOLN1 (mucolipin 1) (e.g., Mucolipidosis, type IV) gene analysis, common variants (e.g., IVS3-2A>G, del6.4kb)
81330	SMPD1(sphingomyelin phosphodiesterase 1, acid lysosomal) (e.g., Niemann-Pick disease, Type A) gene analysis, common variants (e.g., R496L, L302P, fsP330)
81329	SMN1 (survival of motor neuron 1, telomeric) (eg, spinal muscular atrophy) gene analysis; dosage/deletion analysis (eg, carrier testing), includes SMN2 (survival of motor neuron 2, centromeric) analysis, if performed
81336	SMN1 (survival of motor neuron 1, telomeric) (eg, spinal muscular atrophy) gene analysis; full gene sequence
81337	SMN1 (survival of motor neuron 1, telomeric) (eg, spinal muscular atrophy) gene analysis; known familial sequence variant(s)
81412	Ashkenazi Jewish associated disorders (e.g., Bloom syndrome, Canavan disease, cystic fibrosis, familial dysautonomia, Fanconi anemia group C, Gaucher disease, Tay-Sachs disease), genomic sequence analysis panel, must include sequencing of at least 9 genes, including ASPA, BLM, CFTR, FANCC, GBA, HEXA, IKBKAP, MCOLN1, and SMPD1
81420**	Fetal chromosomal aneuploidy (e.g., trisomy 21, monosomy X) genomic sequence analysis panel, circulating cell-free fetal DNA in maternal blood, must include analysis of chromosomes 13, 18, and 21
81507**	Fetal aneuploidy (trisomy 21, 18, and 13) DNA sequence analysis of selected regions using maternal plasma, algorithm reported as a risk score for each trisomy
81511	Fetal congenital abnormalities, biochemical assays of four analytes (AFP, uE3, hCG [any form], DIA) utilizing maternal serum, algorithm reported as a risk score (may include additional results from previous biochemical testing)

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APPROVAL HISTORY

February 1, 2007: Reviewed by the Clinical Coverage Criteria Committee

Subsequent endorsement date(s) and changes made:

- January 30, 2008: Comparative genomic hybridization through microarray analysis and Preimplantation Genetic Determination limitations were removed from this guideline.
- February 11, 2009: For an April 1, 2009 effective date – new codes added.
- August 5, 2009: For a January 1, 2010 effective date: S3870 added to MNG.
- February 1, 2010: Reviewed by Medical Specialty Policy Advisory Committee (MSPAC), no changes.
- March 2011: Reviewed at MSPAC, no changes.
- January 1, 2012: New CPT codes added.

- March 7, 2012: Reviewed by Integrated Medical Policy Advisory Committee (IMPAC), no changes.
- December 20, 2012: Codes 81161, 81324, 81325, 81326, 81479 added to the Medical Necessity Guideline as requiring Prior Authorization, effective January 1, 2013.
- December 11, 2013: Reviewed by IMPAC, coding updated effective January 1, 2014
- July 25, 2014: Reviewed by IMPAC for effective date of November 1, 2014, added information regarding the use of Interqual®
  Molecular Diagnostics criteria as a reference for the review of all genetic/molecular testing requests.
- August 29, 2014: Additional clarification language related to November 1, 2014 notice. Added codes already requiring review/prior authorization not previously listed (81599, 84999, 81370-81377, 81206-81208).
- September 10, 2014: IMPAC voted to maintain internally developed medical necessity guidelines for BRCA, Cancer of Unknown Primary, Retinoblastoma.
- September 30, 2014: Adopted by Tufts Health Plan – Network Health Commercial Plans and Tufts Health Plan – Network Health Medicaid Plans.
- October 16, 2014: Change to effective date for use of Interqual® Molecular Diagnostics criteria from November 1, 2014 to February 1, 2015.
- November 19, 2014: Reviewed by IMPAC, update to overview section. Links to Noncovered Investigational Services (NCIS) and Genetic Testing Request Form added. Instructions for finding Clinical Evidence Summaries added. Added specification for requests from laboratories. Added disclaimer points regarding code lists: e.g., list may not be all inclusive, deleted codes and codes not effective are not reimbursable. Added 81235, status change from NCIS to requiring Prior Authorization. Added 81287 back to this guideline after resolution of discrepancy with programming status. Added the following codes from Medical Necessity Guidelines to be retired due to change to Interqual® criteria: 81201-81203, 81210, 81241, 81243, 81244, 81275, 81280, 81282, 81292-81300, 81302-81304, 81317-81319, 81331, 83890-83898, 83900-83906, 83912, 84999, 86386, 89290, 89291, S3833, S3834, S3845, S3846, S3854, S3861, S3870. Added codes that do not require prior authorization for reference.
- January 1, 2015: Coding updated per AMA CPT® for effective date 2/1/15. The following codes added: 81246, 81288, 81410, 81411, 81435, 81436, 81519.
- January 22, 2015: Change to effective date for use of Interqual® Molecular Diagnostics criteria from February 1, 2015 to March 2, 2015.
- January 23, 2015: Coding updated per AMA CPT®, 1/1/15 coding changes, for effective date 3/2/15. The following code added: 81420.
- January 26, 2015: Codding updated. CPT codes 81221, 81222, 81223 and 81224 added to list of codes which do not require prior authorization for clarification of CF testing.
- June 10, 2015: Coverage of CPT codes 81321, 81322 and 81323 reviewed by IMPAC. Effective October 1, 2015, status change from non-covered investigational service to prior authorization required.
- August 12, 2015: Reviewed by Integrated Medical Policy Advisory Committee (IMPAC). Effective September 21, 2015 Genetic Testing, Retinoblastoma MNG will be retired. Refer to InterQual® Clinical Evidence Summary, Retinoblastoma. Applicable coding updated.
- September 2015: Branding and template change to distinguish Tufts Health Plan products in "Applies to" section. Added Tufts Health Freedom Plan products, effective January 1, 2016.
- October 14, 2015: Reviewed at IMPAC. Effective April 1, 2016, Afirma Thyroid FNA Analysis to be covered with prior authorization
- December 9, 2015: Reviewed by IMPAC. For effective date April 1, 2016, refer to "Array-based Cytogenetic Testing for Detection of Chromosomal Abnormalities" Clinical Evidence Summary for Genomic Microarray Analysis Testing for Intellectual Disability, Developmental Delay, Multiple Congenital Anomalies, and Autism Spectrum Disorders . For effective date July 1, 2016, clarification of molecular diagnostics and genetic testing will be added. Additional criteria added will require genetic counseling by a board certified genetic counselor or MD geneticist and will allow requests from MD's with expertise in targeted disease. Repeat genetic testing will be added to limitations section. Coding updated per AMA CPT® coding changes and description. Effective 12/9/15 CPT 89290, 89291, S3833 and S3834 removed. Refer to Preimplantation Genetic Determination MNG for CPT 89290 and 89291.

- December 31, 2015: Coding updated. Per AMA CPT®, effective December 31, 2015 the following code(s) deleted: S3854; and effective January 1, 2016 the following code(s) added: 81170, 81218, 81219, 81272, 81273, 81276, 81311, 81314, 81412, 81437, 81438
- February 11, 2016: Afirma Thyroid FNA Analysis (CPT 81545) covered with prior authorization
- March 9, 2016: Reviewed by IMPAC: Additional criteria added for effective date of 7/1/16 will require that patient history, physical examination and conventional diagnostic testing do not result in a definitive diagnosis of suspected disorder. Limitation of genetic testing panels added for effective date of 7/1/16. Effective 7/1/16, myRisk® Hereditary Cancer test will be covered with prior authorization. Effective 7/1/16 CPT 81235 will be covered without prior authorization.
- July 1, 2016: Coding updated. S3854 re-instated.
- October 28, 2016: Coding table added to clarify accepted CPT code(s) for myRISK™ Hereditary Cancer Test and myRISK™ Update Test, prior authorization request.
- December 14, 2016: Reviewed by IMPAC, renewed without changes.
- December 14, 2016: ThyroSeq® Next Generation Sequencing reviewed by IMPAC. Effective January 10, 2017, ThyroSeq® (CPT 81479) is covered with prior authorization.
- December 31, 2016: Coding updated. Per AMA CPT®, effective December 31, 2016 the following code(s) deleted: 81280, 81281, 81282 and effective January 1, 2017 the following code(s) added: 81413, 81414, 81439.
- April 12, 2017: Reviewed by IMPAC. Addition to limitation section, genetic tests whose clinical utility is scientifically unproven with added link to Noncovered Investigational Services MNG. Language change (scientifically added) to coincide with change to EOC language. Links added to Genetic Testing: Maternal Tests for Fetal Trisomy MNG and Genetic Testing: Prenatal, Preconception MNG.
- April 2017: Added RITogether Plan product to template. For MNGs applicable to RITogether, effective date is August 1, 2017.
- August 1, 2017: For effective date August 1, 2017, Interqual SmartSheets to be submitted with Genetic and Molecular Diagnostics Testing Authorization Request Form. Coding updated. The following ICD-10-CM and HCPCS codes are added: 0016U, 0017U, S3850.
- October 1, 2017: Coding updated. For effective date October 1, 2017, the following ICD-10-CM codes are added: 0022U, 0023U.
- December 13, 2017: Reviewed by IMPAC, renewed without changes. CPT 81434 will be covered with prior authorization.
- December 31, 2017: Coding updated. Per AMA CPT®, effective January 1, 2018 the following code(s) added: 81107. 81108, 81109, 81110, 81111, 81112, 81120, 81121, 81175, 81176, 81238, 81247, 81248, 81249, 81258, 81259, 81269, 81283, 81334, 81361, 81362, 81363, 81364, 81521, 81541, 0026U, 0027U.
- January 16, 2018: CPT 81434 added to list of CPT/HCPCS codes requiring prior authorization.
- May 31, 2018: Code description updated.
- June 26, 2018: Coding updated. Per AMA CPT®, effective July 1, 2018 the following code(s) added: 0046U, 0049U.
- September 12, 2018: Reviewed By IMPAC. Clarification to criteria when genetic test will directly alter the treatment and/or medical management of a condition which has been clinically diagnosed. Link to Prenatal, Preconception MNG added to limitations section.
- October 1, 2018: Coding updated. Per AMA CPT®, effective October 1, 2018 the following code(s) added: 0069U.
- October 2018: Template and disclaimer updated
- December 3, 2018: 2018.2 Interqual upgrade for Tufts Health Commercial products including Tufts Health Freedom Plan. Effective December 17, 2018, Interqual upgrade is effective for Tufts Health Direct and Tufts Health Together. Effective January 14, 2019, Interqual upgrade effective for Tufts Health RITogether.
- December 31, 2018: Coding updated. Per AMA CPT®, effective January 1, 2019 the following code(s) added: 81171, 81172, 81173, 81174, 81177, 81178, 81179, 81180, 81181, 81182, 81183, 81184, 81185, 81186, 81187, 81188, 81189, 81190, 81204, 81233, 81234, 81236, 81237, 81239, 81271, 81274, 81305, 81320, 81333, 81343, 81344, 81345.
- April 25, 2019: Effective April 25, 2019, 2018 Interqual upgrade includes Interqual smartsheets Thyroid Nodule Genetic Testing : Afirma MTC Classifier and Thyroid Nodule Genetic Testing: Multi-gene panel for thyroid nodule
- July 17, 2019: Reviewed at IMPAC. THP modification to Interqual thyroid nodule testing criteria added. A repeat FNA of thyroid nodule is not required when initial FNA cytology result indicates

Bethesda IV, suspicious for follicular or Hürthle cell neoplasm (SFN/SHCN) or follicular neoplasm (FN)
- September 18, 2019: Reviewed at IMPAC. Effective January 1, 2020, CPT 81443 requires prior authorization.
- November 20, 2019: Reviewed by IMPAC. For effective date November 20, 2019, CPT 81445 added and may be covered with prior authorization for NSCLC diagnosis. CPT 81450 added and may be covered with prior authorization for AML diagnosis. For effective date April 1, 2020, CPT 81337 will require prior authorization. For effective date April 1, 2020, CPT 81337 will require prior authorization.
- January 1, 2020: Coding updated. Per AMA CPT®, effective January 1, 2020 the following code(s) added: 81307, 81308, 81309, 0154U, 0155U
- January 6, 2020: Coverage of CPT 81337, SMN1 (survival of motor neuron 1, telomeric) (eg, spinal muscular atrophy) gene analysis; known familial sequence variant(s)) reviewed by IMPAC voting committee. CPT 81337 will remain covered and will not require prior authorization effective April 1, 2020. For clarification, CPT 81329, 81336 and 81337 added to MNG under genetic testing covered without prior authorization.
- February 19, 2020: Reviewed at IMPAC. THP Modification to InterQual criteria for thyroid nodule testing added: Section 10: Bethesda III, atypia or follicular lesion of undetermined significance (AUS/FLUS) Criteria 1.A- Repeat FNA is not required (consider criteria point met)
- July 1, 2020: Coding updated. Per AMA CPT®, effective July 1, 2020 the following code(s) added:0172U, 0177U.
- July 9, 2020, Fax number for Unify updated.
- July 29, 2020: Reference to Medical Necessity Guidelines: BRCA-Related Breast and/or Ovarian Cancer Syndrome removed from CPT 0172U.
- September 16, 2020: Reviewed by IMPAC, renewed without changes.
- December 31, 2020: Coding updated. Per AMA CPT®, effective December 31, 2020 the following code(s) deleted: 81545 and effective January 1, 2021 the following code(s) added: 81168, 81191, 81192, 81193, 81194, 81278, 81279, 81338, 81339, 81347, 81348, 81351, 81352, 81353, 81357, 81360.

BACKGROUND, PRODUCT AND DISCLAIMER INFORMATION

Medical Necessity Guidelines are developed to determine coverage for benefits, and are published to provide a better understanding of the basis upon which coverage decisions are made. We make coverage decisions using these guidelines, along with the Member's benefit document, and in coordination with the Member's physician(s) on a case-by-case basis considering the individual Member's health care needs.

Medical Necessity Guidelines are developed for selected therapeutic or diagnostic services found to be safe and proven effective in a limited, defined population of patients or clinical circumstances. They include concise clinical coverage criteria based on current literature review, consultation with practicing physicians in our service area who are medical experts in the particular field, FDA and other government agency policies, and standards adopted by national accreditation organizations. We revise and update Medical Necessity Guidelines annually, or more frequently if new evidence becomes available that suggests needed revisions.

For self-insured plans, coverage may vary depending on the terms of the benefit document. If a discrepancy exists between a Medical Necessity Guideline and a self-insured Member's benefit document, the provisions of the benefit document will govern.

Treating providers are solely responsible for the medical advice and treatment of Members. The use of this guideline is not a guarantee of payment or a final prediction of how specific claim(s) will be adjudicated. Claims payment is subject to eligibility and benefits on the date of service, coordination of benefits, referral/authorization, utilization management guidelines when applicable, and adherence to plan policies, plan procedures, and claims editing logic.

Provider Services